

Genesis, frequency, and diagnostic significance of ejection sound in adults with tetralogy of Fallot

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The clinical records of 24 adult patients with tetralogy of Fallot showed an ejection sound to be present in 13, 12 of whom had significant pulmonary valvular stenosis. In 10 patients with infundibular obstruction only, an ejection sound was recorded in one. The pulmonary closure sound was recorded in all patients having an ejection sound, but in only 4 of 11 patients without an ejection sound. The ejection sound was clearly recorded with a catheter-tip micromanometer in the proximal pulmonary artery where it occurred coincident with an anacrotic notch, 40 msec after the rise of pulmonary artery pressure. Angiograms showed doming of the stenotic pulmonary valve. A pulmonary ejection sound was recorded in presystole in one patient when the right ventricular end-diastolic pressure, due to a forceful atrial contraction, exceeded the pulmonary artery pressure; during a short period of atrioventricular dissociation, the timing of the ejection sound varied as a function of the PR interval. Therefore an ejection sound occurs frequently in adults with tetralogy of Fallot, where it is a diagnostically useful sign, indicating the presence of pulmonary valvular stenosis.

In infants and children with tetralogy of Fallot the incidence of ejection sounds varies directly with the severity of the pulmonary outflow obstruction. Thus, ejection sounds are stated to be rare in milder forms of tetralogy of Fallot but are frequent in severe and extreme forms (Vogelpoel and Schrire, 1960b; La-fargue *et al.*, 1967; Perloff, 1970). In severe tetralogy of Fallot an ejection sound is thought to originate from a dilated overriding ascending aorta which is not a feature of milder forms (Leatham, 1958; Perloff, 1970). However, in adult patients with either less severe forms of tetralogy of Fallot or in whom the course had been altered by palliative operation, we commonly noted the presence of an ejection sound. There was no apparent correlation between the severity and the presence or absence of an ejection sound which did appear to be present, however, in those patients with valvular pulmonary stenosis. In 8 cases studied prospectively since making this observation, we have been able to make a correct precatheterization diagnosis in 7, i.e. tetralogy of Fallot with or without valvular pulmonary stenosis. Consequently the present study was designed to define more clearly the significance of an ejection sound in adult patients with tetralogy of Fallot.

Subjects and methods

Records of all patients with the diagnosis of tetralogy of Fallot who were studied at this institution since June 1963 were reviewed. For purposes of this study tetralogy of Fallot was defined as the combination of a large ventricular septal defect and right ventricular outflow obstruction resulting in equal right and left ventricular pressures. Patients with a small ventricular septal defect and/or mild right ventricular outflow obstruction were therefore excluded. The phonocardiograms were reviewed by two of the authors (J.A.S. and C.E.M.) and were divided into two groups based on the presence or absence of ejection sound. Satisfactory phonocardiograms were available in 22 patients. Two additional patients (Cases 2 and 24) were accepted without preoperative phonocardiograms because a detailed description of the physical findings by a senior member of the cardiology faculty was available for both.

The haemodynamic, angiographic, and surgical data were then reviewed and grouped according to the presence or absence of pulmonary valvular stenosis. The type of right ventricular outflow tract obstruction was determined by pressure measurements during cardiac catheterization, by angiography, and in 16 patients by direct examination at operation. Patients were classified as having pure valvular stenosis when an additional pressure gradient across the infundibulum was not demonstrable even though the infundibulum may have appeared narrow by angiography or at operation. Angiograms

and/or reports of surgical visualization of the valve were available for all patients. The ejection sound (ES) was then evaluated in terms of its sensitivity, specificity, and overall correctness in predicting the presence or absence of pulmonary valvular stenosis (PVS) according to the following formulae:

$$\text{Sensitivity} = \frac{\text{Patients with both PVS and ES}}{\text{Total with PVS}}$$

$$\text{Specificity} = \frac{\text{Patients with no ES and no PVS}}{\text{Total without PVS}}$$

$$\text{Overall correctness} = \frac{\text{True positives plus true negatives}}{\text{Total patients}}$$

Special catheterization studies

Special catheterization studies were performed on 3 patients who were studied prospectively. Sound-pressure correlations of the ejection sound were made with Dallons-Telco catheter-tip micromanometers. External sound was recorded along with selected sound pressure measurements from the right and left ventricle, pulmonary artery, central aorta, and, in one instance, from the right atrium. One patient with valvular pulmonary stenosis with intact ventricular septum was studied in a similar manner. The tracings were analysed as previously described for evaluation of heart sounds in relation to pressure events (Whittaker *et al.*, 1969).

TABLE I Summary of clinical findings in patients with tetralogy of Fallot

Case No.	Age (yr)	Sex	Site of obstruction*	NYHA FC†	Ejection click present		Arterial O ₂ saturation (%)	Palliative operation	Associated lesions
					Pulmonary closure recorded	Murmur duration (% distance to aortic closure)			
Ejection click present									
1	22	F	Valve	I	Yes	100	80	None	Mild aortic insufficiency
2	21	F	Valve	II	Yes	50	73	Blalock at 9 yr	None
3	19	M	Valve	I	Yes	100	88	Potts at 5 yr	None
4	33	M	infundibular	III	Yes	100	88	None	None
5	38	F	Valve	III	Yes	100	Hct. 78%	None	None
6	18	M	infundibular	IV	Yes	70	82	Brock at 5 yr	None
7	48	M	Valve	I	Yes	80	—	None	None
8	41	F	infundibular	II	Yes	100	85	Potts at 21 yr	None
9	40	F	Valve	I	Yes	100	90	None	None
10	39	M	Valve	I	Yes	70	72	None	Aortic stenosis, persistent ductus arteriosus
11	20	F	infundibular	I	Yes	100	84	Blalock at 7 yr	None
12	19	F	Valve	III	Yes	100	86.5	Potts at 4 yr	None
13	17	M	Infundibular	II	Yes	80	81	Blalock at 5 yr	None
Ejection click absent									
14	19	F	Valve	o	No	100	91	Blalock and Brock at 6 yr	None
15	26	M	infundibular	III	No	90	70	None	None
16	19	M	Valve	I	No	100	—	Brock at 5 yr	Pulmonary branch stenosis (rubella)
17	16	M	Infundibular	o	Yes (faint)	70	—	Potts at 18 mth	Minimal aortic insufficiency
18	19	M	Infundibular	II	Yes (faint)	100	90	Brock	None
19	17	M	Infundibular	III	No	60	—	None	None
20	19	F	Infundibular	II	No	70	—	Blalock at 4½ yr	None
21	29	F	Infundibular	II	No	70	88	None	Persistent ductus arteriosus
22	40	F	Infundibular	I	Yes	100	88	None	Mild pulmonary insufficiency
23	22	M	Infundibular	II	Yes (faint)	100	—	Blalock at 6 yr	None
24	17	M	Infundibular	I	No	70	86	Blalock at 6 and 8 yr	None

*In patients with only valve obstruction the infundibular appeared narrow on the angiogram and at operation but no pressure gradient was demonstrated across the infundibular outflow tract.

† New York Heart Association functional classification.

Results

Studies were made on 14 male and 10 female patients ranging in age from 16 to 48 years (mean 26 years). The clinical and haemodynamic data are summarized in Table 1. Fourteen had pulmonary valve stenosis comprising part or all of the obstruction; 14 had previous palliative procedures; and 6 had associated cardiac anomalies. All but one patient (Case 22) had a history of cyanosis which was still present at least intermittently in 6 patients (Cases 2, 5, 6, 15, 19, 21). Two patients (Cases 14 and 17) were asymptomatic at the time of study and one (Case 6) was severely symptomatic with dyspnoea and fatigue at rest. Nine were considered to be in the New York Heart Association Functional Class I, 7 in Functional Class II, and 5 in Functional Class III.

Relation between ejection sound and type of right ventricular outflow obstruction

An ejection sound was present in 13 patients (Fig. 1) (Table 2). In 12 patients with an ejection sound there was pulmonary valve stenosis, associated with significant infundibular obstruction in 6. The pulmonary valve was normal in one patient in whom an

ejection sound was present. An ejection sound was absent in 11 patients (Fig. 2) in 9 of whom there was no pulmonary valve stenosis. Of the 2 patients with pulmonary valve stenosis and no ejection sound, one had associated infundibular obstruction and one had additional pulmonary branch stenosis. The association between the site of obstruction and the presence or absence of an ejection sound is shown in Table 2. Using the numbers from Table 2, calculations were made of sensitivity, specificity, and overall correctness for the pulmonary ejection sound as an indicator of the presence or absence of pulmonary valvular stenosis in adult tetralogy of Fallot, therefore:

$$\text{Sensitivity} = \frac{\text{Number with both PVS and ES}}{\text{Total with PVS}} = \frac{12}{14} = 86\%$$

with a 14% incidence of false negatives

$$\text{Specificity} = \frac{\text{Number with neither PVS nor ES}}{\text{Total without PVS}} = \frac{9}{10} = 90\%$$

with a 10% incidence of false positives

$$\text{Overall correctness} = \frac{\text{True positives and true negatives}}{\text{Total number}} = \frac{12 + 9}{24} = 88\%$$

The interval from the Q wave of the electrocardiogram to the ejection sound (Q-ES) varied from 80

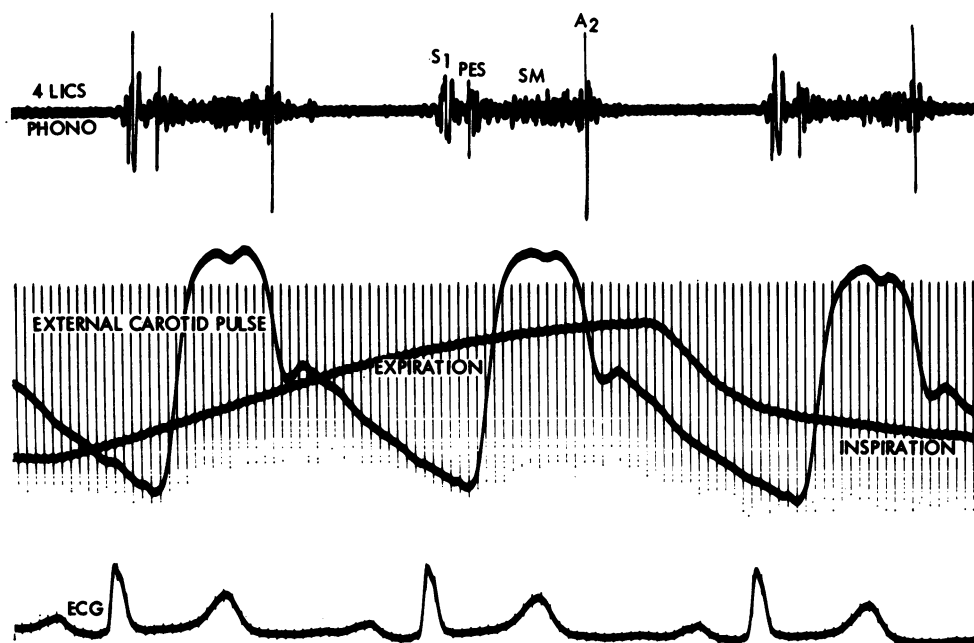


FIG. 1 Phonocardiogram from Case 12 with valvular pulmonary stenosis and an ejection sound (PES). The Q-PES interval measures 120 msec. The systolic murmur (SM) extends to the aortic closure sound (A_2). A faint pulmonary closure sound is recorded only in the first complex, separated from A_2 by 85 msec. In this and subsequent phonocardiograms paper speed = 100 mm/sec and time lines = 20 msec.

TABLE 2 *Relation of ejection sound to selected clinical characteristics*

<i>Ejection sound</i>	<i>Pulmonary valve stenosis</i>		<i>Pulmonary closure recorded</i>		<i>Previous palliative operation</i>	
	<i>Present</i>	<i>Absent</i>	<i>Yes</i>	<i>No</i>	<i>Yes</i>	<i>No</i>
Present (N=13)	12	1	13	0	7	6
Absent (N=11)	2	9	4	7	7	4
Total (24)	14	10	17	7	14	10

to 130 msec (mean 101 msec), excluding one (Case 10) in which it occurred before the onset of QRS (see below). Externally the ejection sound was usually recorded best at the upper left sternal border and showed no consistent variation with respiration (Fig. 3).

Relation between ejection sound and pulmonary closure sound

The pulmonary component of second heart sound (P_2) was recorded or heard in 17 of 24 patients (Table 2). It was recorded in all patients in whom an ejection sound was present, but was absent in 7 of 11 patients who did not have an ejection sound. P_2 was present in 12 of 14 patients with valvular pulmonary stenosis. In 10 patients with only infundibular stenosis in contrast, P_2 was absent in 5, recorded intermittently in 3, and recorded well in only 2. Splitting between aortic closure and P_2

ranged from 30 to 115 msec (mean 71 msec) and showed no consistent narrowing during expiration.

Relation between previous palliative operation and an ejection sound

Of 14 patients with previous palliative operations, an ejection sound was present in 7 and absent in 7 (Table 2). A history of previous palliative operation showed no relation therefore to the presence or absence of an ejection sound.

Results of sound pressure correlation studies

Sound pressure recordings were made from the ventricles and central aorta in 3 patients. The catheter was then advanced into the pulmonary artery and simultaneous pulmonary artery and left ventricular or central aorta measurements were made. In the central aorta and ventricles the first heart sound was clearly recorded and was accompanied by a transient

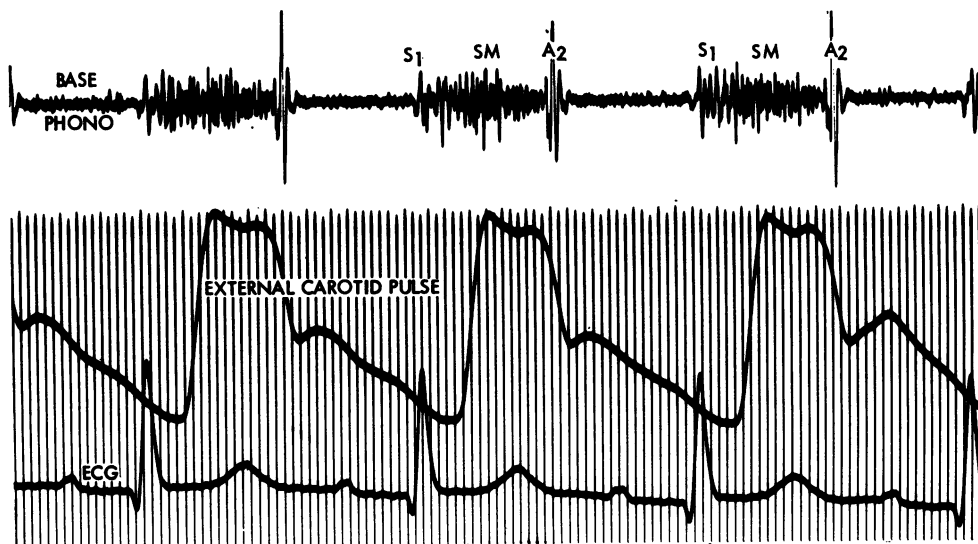


FIG. 2 Phonocardiogram from Case 10 with tetralogy and pulmonary infundibular stenosis. The absence of an ejection and a pulmonary closure sound and the presence of a long systolic murmur are characteristic of this type of tetralogy which is of mild to moderate severity.

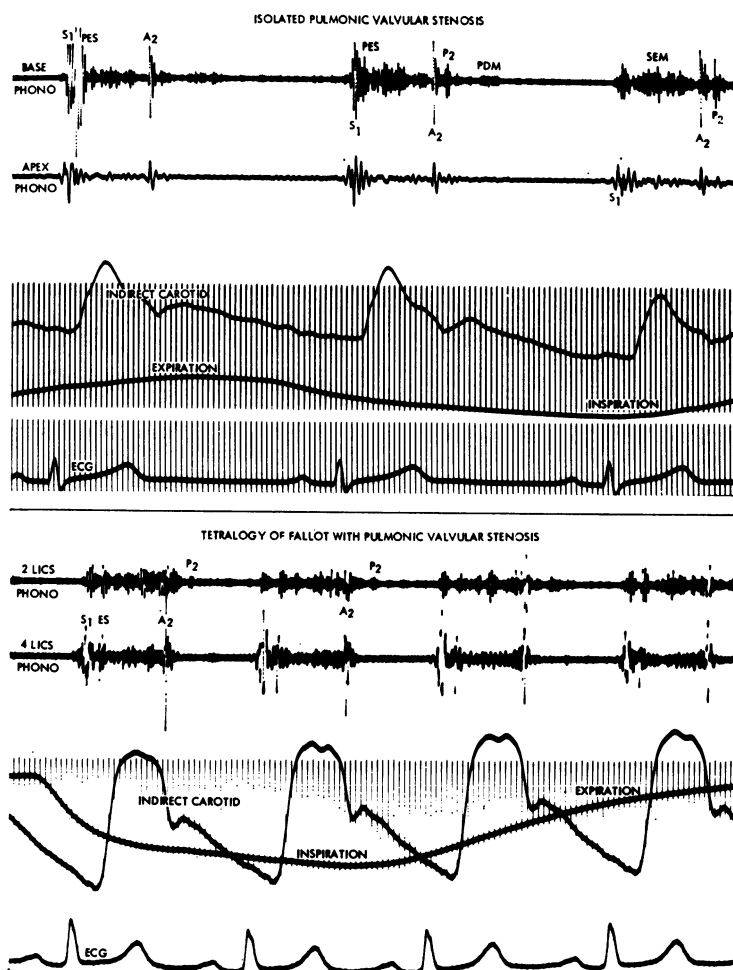


FIG. 3 Phonocardiograms demonstrating the effect of respiration on the intensity of an ejection sound. In pulmonary valvular stenosis with an intact ventricular septum (top panel), the ejection sound decreases in intensity during inspiration. In pulmonary valvular stenosis associated with tetralogy of Fallot (bottom panel), no respiratory variation in intensity of the ejection sound was noted. Respirations are recorded with a thermistor.

in the central aorta pressure tracing (Fig. 4-5). The ejection sound was recorded poorly in the ventricles and central aorta. It was recorded externally after the onset of pressure rise in the central aorta but was not accompanied by a transient in the pressure tracing. When the micromanometer was advanced into the pulmonary artery, a prominent pulmonary ejection murmur was recorded. The ejection sound on the external recording diminished in intensity but was clearly recorded from the pulmonary artery catheter. It occurred 30 to 40 msec after the onset of pressure rise in the pulmonary artery accompanied by an anacrotic notch (Fig. 5).

In one patient (Case 10) a sharp ejection sound was recorded before the onset of the QRS complex, 150 msec after the P wave. It was best recorded externally in the second intercostal space and poorly at the apex (Fig. 6). This patient had associated aortic valvular stenosis with a 40 mm left ventricular central aorta gradient and a persistent ductus arteriosus. The relation of the presystolic sound to atrial contraction was shown during a transient period of atrial-ventricular dissociation which followed two spontaneous premature ventricular contractions (Fig. 6). With a normal PR interval a prominent presystolic sound was recorded at the base. During

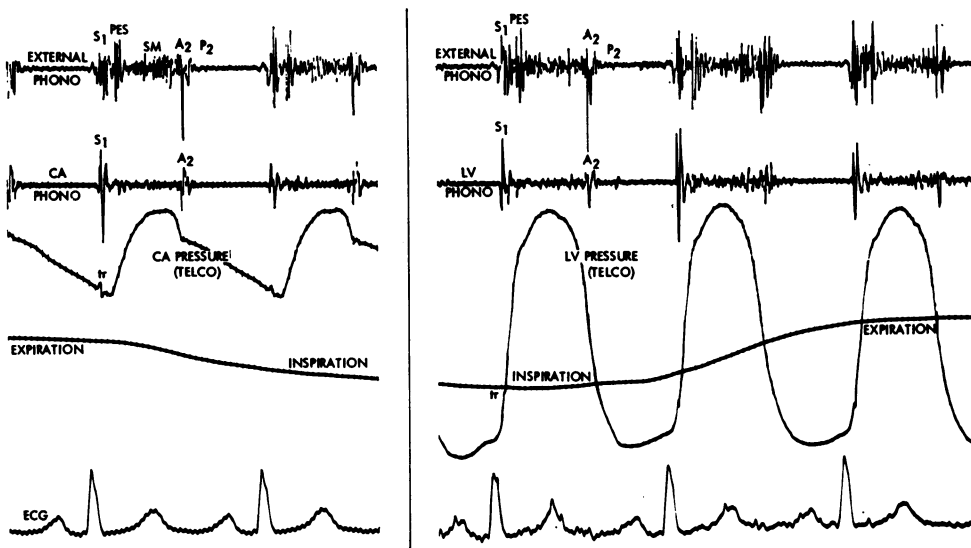


FIG. 4 Correlation of sound and pressure using a catheter-tip micromanometer in Case 11 who has tetralogy of Fallot, and valvular pulmonary stenosis. On the left panel, the catheter is placed immediately above the aortic valve (CA). A prominent first heart sound (S_1) and a transient (tr), but no systolic murmur (SM) or ejection sounds are recorded by the CA microphone. An ejection sound (PES) is recorded externally. On the right panel, the catheter has been advanced into the left ventricle (LV). A transient (tr) is seen on the LV pressure trace coincident with S_1 . An ejection sound is recorded externally but not from the LV.

subsequent beats the timing of the sound appears as a function of the PR interval, occurring in early systole when the PR interval is short and gradually emerging into presystole as the PR interval lengthens. During catheterization the sound was shown to occur when the right atrial a wave of 8 mm amplitude (and therefore right ventricular end-diastolic pressure) exceeded the pulmonary artery pressure (Fig. 7). When the patient experienced a vasovagal attack with diaphoresis and nausea during catheterization, the presystolic sound disappeared and the right ventricular a wave dropped below the pulmonary artery end-diastolic pressure.

In a patient with pulmonary valvular stenosis and an intact ventricular septum, an ejection sound occurred 30 to 40 msec after pulmonary artery right ventricular pressure crossover, coincident with the anacrotic notch in the pulmonary artery (Fig. 8).

Discussion

An ejection sound may originate from the aortic root, from the pulmonary outflow tract, or from an abnormal aortic or pulmonary valve (Wolferth and Margolies, 1945; Leatham and Vogelpoel, 1954; Whittaker *et al.*, 1969; Hultgren *et al.*, 1969). In severe tetralogy of Fallot it is thought to arise from a dilated, anteriorly overriding ascending aorta.

Another explanation is required for the high frequency of ejection sounds in the present group of patients who seemed to have a less severe form of tetralogy, in which a much dilated anteriorly overriding aorta and an aortic ejection sound are not present (Vogelpoel and Schrire, 1960b; Gotsman, 1966; Friesinger and Bahnson, 1966).

We considered this group of patients to have less severe forms of tetralogy on the basis of survival into adulthood with only moderate symptoms, long systolic murmurs, and lack of severe cyanosis (Vogelpoel and Schrire, 1960b). This distinction is not easily made since some patients with severe pulmonary outflow obstruction may do well clinically because of extensive development of bronchial collateral circulation (Bing, Vandam, and Gray, 1947; Higgins and Mulder, 1972). In addition, the degree of infundibular obstruction may increase with time, accounting for a delayed appearance of symptoms in some patients (Gotsman, 1966).

It was also considered that previous palliative operation might have obscured a very severe tetralogy with a dilated overriding aorta in some of our patients. If an ejection sound originated from a dilated aorta in these patients, however, one would expect a higher incidence of ejection sounds among those patients who had previous palliative

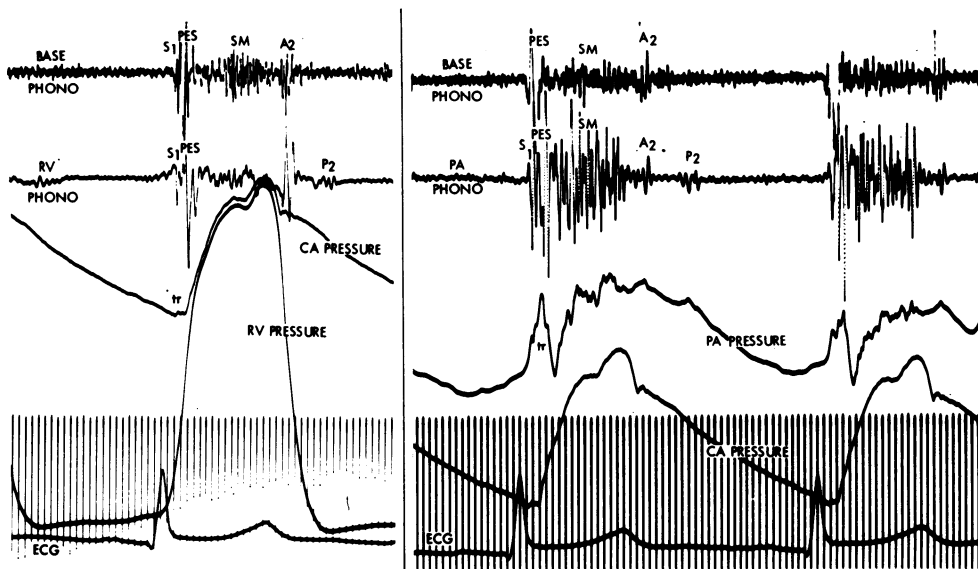


FIG. 5 Sound-pressure correlations with catheter-tip micromanometer (Case 8). Left panel: right ventricular (RV) and central aorta (CA) pressures are recorded by equisensitive catheters. A transient (tr) appears on the CA pressure trace coincident with S_1 . A tr does not accompany the ejection sound (PES) which is recorded by both the external and RV phonos. The RV phono is positioned immediately under the pulmonary valve. Right panel: The RV catheter has been advanced to the pulmonary artery (PA). PES is now less prominent on the external phonocardiogram. It is recorded along with a loud systolic murmur by the PA microphone, and is coincident with tr on the PA pressure trace. Sensitivity of the PA catheter has been increased and the CA pressure trace has been lowered.

operations (McKusick, 1958). Patients who had palliative operations, however, were found to be equally divided into the groups with and without an ejection sound (Table 2).

Tetralogy of Fallot patients with pulmonary valvular stenosis have been noted previously (Vogelpoel and Schrire, 1960b), as in the present study, to have a higher incidence of a recordable pulmonary valve closure sound. This indicates that the pulmonary valve, though stenotic, was mobile and that the diastolic pulmonary artery pressure was adequate to account for a pulmonary closure sound.

The aetiology and behaviour of the ejection sound in adults with tetralogy of Fallot may be studied by comparing it with that of patients with pulmonary stenosis and an intact ventricular septum. An ejection sound is conspicuously absent in isolated infundibular pulmonary stenosis, but is a usual feature of mild and severe grades of valvular stenosis, though in more severe forms it may merge with the first heart sound (Vogelpoel and Schrire, 1960a; Gamboa, Hugenholtz, and Nadas, 1964; Perloff, 1964). In isolated pulmonary valve stenosis, an ejection

sound has been postulated to arise from the valve proper or from the snapping of the dilated post-stenotic portion of the pulmonary artery during early ejection (Leatham and Weitzman, 1957). Recent studies using simultaneous recordings of electrocardiographic, angiographic, and sound pressure recordings have shown the ejection sound to appear simultaneously with an abrupt doming of the stenotic valve, before the wall of the pulmonary artery distends (Hultgren *et al.*, 1969). Therefore, a mobile doming stenotic valve appears to be the primary cause of the ejection sound in pulmonary valve stenosis. An angiogram showing doming of the stenotic pulmonary valve in a patient (Case 11) with tetralogy of Fallot, pulmonary valve stenosis, and an ejection click is shown in Fig. 9. At the onset of ejection the upward excursion of the stenotic valve was seen to check abruptly during angiography as has been described in patients with aortic and isolated pulmonary valvular stenosis (Epstein *et al.*, 1965; Whittaker *et al.*, 1969; Hultgren *et al.*, 1969). This is the likely explanation for an ejection sound in adult patients with tetralogy of Fallot in whom

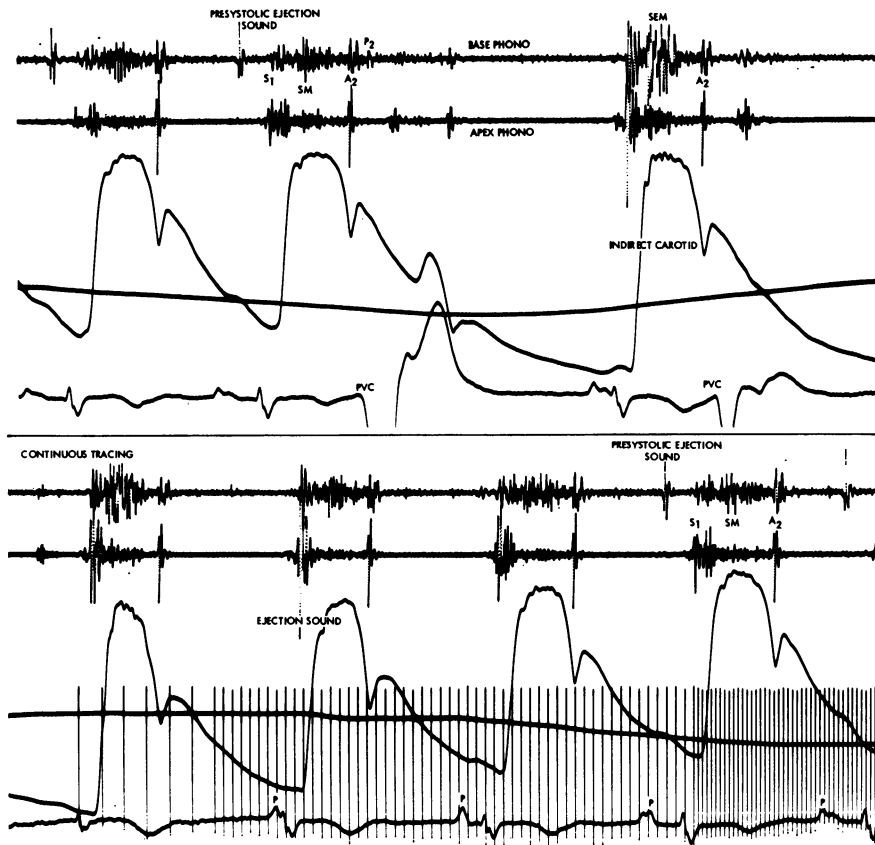


FIG. 6. External phonocardiogram (Case 10) showing a presystolic ejection sound during sinus rhythm (top panel, first two complexes). When a transient junctional escape rhythm occurs after the premature ventricular contraction (PVC) the ejection sound disappears from presystole. The presystolic sound reappears (bottom panel) with gradual lengthening of the PR interval; following the p wave by 120 msec. Time lines = 40 msec in middle of bottom panel and 20 msec on right bottom panel.

post-stenotic dilatation of the pulmonary artery is not a usual feature.

Although ejection sounds of isolated pulmonary valve stenosis often decrease in intensity during inspiration (Reeve, 1966), this was not observed in our patients with tetralogy of Fallot (Fig. 3). In isolated pulmonary valve stenosis, the pressure difference between the right ventricle and the pulmonary artery may narrow when the right atrial a wave is accentuated by an inspiratory increase in venous return. As a result the pulmonary valve is already in a domed position at the onset of right ventricular systole during inspiration and the intensity of the ejection sound is diminished (Hultgren *et al.*, 1969).

In tetralogy of Fallot, in contrast, the right atrial a wave is not accentuated (Hoffman *et al.*, 1960). The large ventricular septal defect provides a runoff

for the increased venous return into the left ventricle, thereby preventing a significant inspiratory increase in right ventricular end-diastolic pressure. Palliative shunting procedures which direct flow into the pulmonary artery may also prevent an obvious inspiratory drop in pulmonary artery pressure in some patients. Either or both of these factors could explain the lack of respiratory variation which was evident in this group of patients.

The ejection sound of isolated valvular pulmonary stenosis may occur in presystole due to a forceful right atrial contraction which raises right ventricular end-diastolic pressure above that of the pulmonary artery (Hultgren *et al.*, 1969). Though this phenomenon normally does not occur in tetralogy of Fallot because the 'right atrial kick' is not prominent (Hoffman *et al.*, 1960), it was present in Case 10

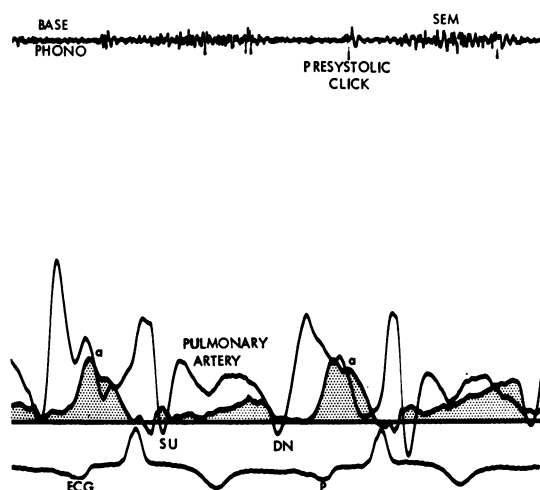


FIG. 7 Simultaneous phonocardiograms, pulmonary arterial and right atrial pressure (dotted area) from Case 10. The presystolic click occurs when the right atrial a wave and therefore right ventricular end-diastolic pressure exceeds pulmonary artery diastolic pressure. The diastolic notch (DN) and systolic upstroke (SU) of the pulmonary artery pressure trace are falsely low reflecting catheter artefact.

who had associated aortic stenosis which may decrease diastolic left ventricular compliance. This sound was a function of the timing of atrial systole as shown in Fig. 6. During escape rhythm, in the absence of a preceding atrial contraction, it appeared as a systolic ejection sound, but returned to presystole as the PR interval progressively lengthened. The haemodynamic determinants of this behaviour were clarified during cardiac catheterization. The presystolic ejection sound occurred when the right atrial a wave (and right ventricular end-diastolic pressure) abruptly rose above pulmonary artery diastolic pressure (Fig. 7). It disappeared completely from presystole during a vasovagal attack when the right atrial a wave dropped below the pulmonary artery end-diastolic pressure.

Sound pressure correlations of ejection sound

Previous studies in this laboratory have shown the usefulness of sound pressure correlations with catheter-tip micromanometers for the precise delineation of heart sounds (Whittaker *et al.*, 1969; Thompson *et al.*, 1970. Ejection sounds of valvular origin in aortic stenosis have been distinguished from those of aortic root origin, in that the latter coincide precisely with the onset of pressure rise in

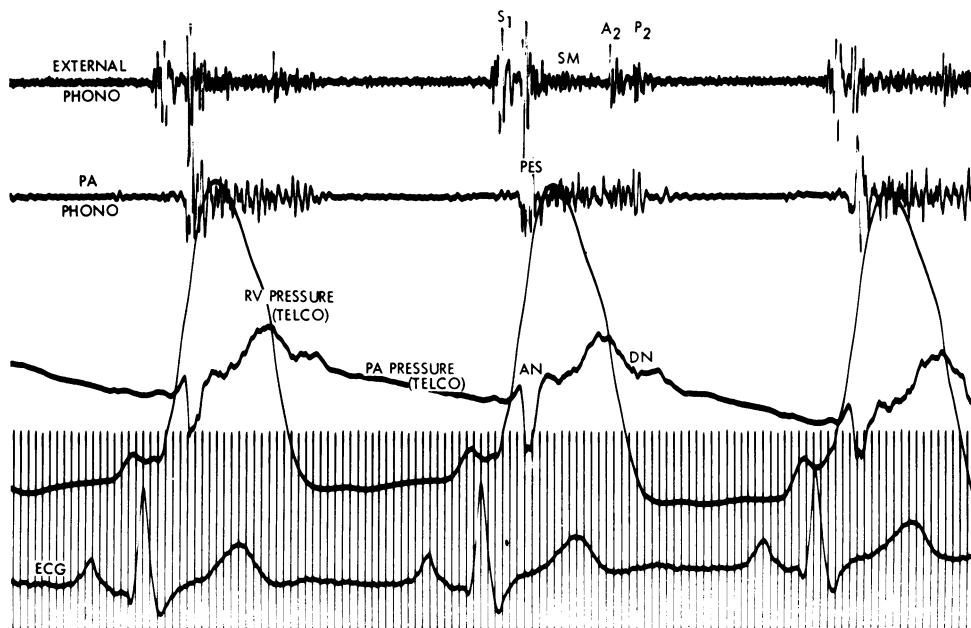


FIG. 8 External and pulmonary artery phonocardiogram showing an ejection sound (PES) in a patient with isolated valvular pulmonary stenosis. As in tetralogy of Fallot with valvular pulmonary stenosis, PES coincides with the anacrotic notch (AN) on the pulmonary artery pressure (PA) tracing.

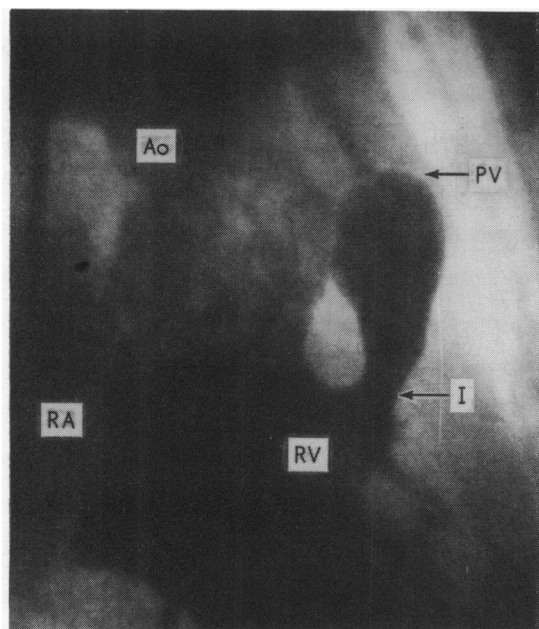


FIG. 9 Right ventricular angiogram in a patient (Case 11) with tetralogy and pulmonary valve stenosis. The doming pulmonary valve (PV) associated with an ejection sound is typical of pulmonary valve stenosis. There is also infundibular (I) narrowing. The aorta (Ao) is beginning to opacify as a result of right-to-left shunting through the large ventricular septal defect.

the central aorta. In contrast, aortic valve ejection sounds occur 20–40 msec after the onset of pressure rise, coincident with an anacrotic notch in the central aorta pressure trace (Whittaker *et al.*, 1969). The ejection sound of isolated valvular pulmonary stenosis was shown to resemble that of valvular aortic stenosis in that it appeared 30–40 msec after the onset of pulmonary artery pressure rise, coincident with the anacrotic notch on the pulmonary artery pressure tracing (Fig. 8). The ejection sound in tetralogy of Fallot was likewise shown to occur after the onset pressure rise, coincident with the anacrotic notch on the pulmonary artery pressure trace (Fig. 5). It was recorded poorly in the right ventricle and central aorta, but clearly in the pulmonary artery in keeping with its postulated pulmonary valve origin (Fig. 4).

In conclusion, ejection sounds may be more common than previously reported in adult patients with mild or moderate forms of tetralogy of Fallot or in whom the clinical course has been altered by previous palliative operations. In this setting, an ejection sound provides strong evidence for the presence of

pulmonary valve stenosis. Though an ejection sound may be present in both, it should be possible at the bedside to distinguish between pulmonary valve stenosis with intact ventricular septum from that associated with mild or moderate tetralogy of Fallot. The lack of respiratory variation of the ejection sound, a small jugular venous a wave (Hoffman *et al.*, 1960), and diminution in intensity of the murmur with amyl nitrate inhalation (Vogelpoel *et al.*, 1959), all favour the presence of tetralogy of Fallot with pulmonary valve stenosis.

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